MicroRNA profiling predicts a variance in the proliferative potential of cardiac progenitor cells derived from neonatal and adult murine hearts.

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Authors: Padmini Sirish, Javier E Lopez, Ning Li, Andrew Wong, Valeriy Timofeyev, J Nilas Young, Maryam Majdi, Ronald A Li, Huei-Sheng Vincent Chen, Nipavan Chiamvimonvat

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Public Summary:
Cardiac progenitor cells (CPCs) are multipotent cells that may offer tremendous potentials for the regeneration of injured myocardium. To expand the limited number of CPCs for effective clinical regeneration of myocardium, it is important to understand their proliferative potentials. Single-cell based assays were utilized to purify c-kit(pos) CPCs from human and mouse hearts. MicroRNA profiling identified eight differentially expressed microRNAs in CPCs from neonatal and adult hearts. Notably, the predicted protein targets were predominantly involved in cellular proliferation-related pathways. To directly test this phenotypic prediction, the developmental variance in the proliferation of CPCs was tested. Ki67 protein expression and DNA kinetics were tested in human and mouse in vivo CPCs, and doubling times were tested in primary culture of mouse CPCs. The human embryonic and mouse neonatal CPCs showed a six-fold increase in Ki67 expressing cells, a two-fold increase in the number of cells in S/G2-M phases of cell cycle, and a seven-fold increase in the doubling time in culture when compared to the corresponding adult CPCs. The over-expression of miR-17-92 increased the proliferation in adult CPCs in vivo by two-fold. In addition, the level of retinoblastoma-like 2 (Rbl2/p130) protein was two-fold higher in adult compared to neonatal-mouse CPCs. In conclusion, we demonstrate a differentially regulated cohort of microRNAs that predicts differences in cellular proliferation in CPCs during postnatal development and target microRNAs that are involved in this transition. Our study provides new insights that may enhance the utilization of adult CPCs for regenerative therapy of the injured myocardium.

Scientific Abstract:
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